–32%, p=0·0008). These phenotypic differences, in combination, could help to explain why south Asian individuals are more susceptible to the adverse metabolic effects of a diet that is both high in fat and energy. Notably, south Asians in the study were shorter and lighter than their Caucasian counterparts, and thus had the same BMI.

Several important questions arise from this study,[6] including what is the exact difference in molecular composition of BAT between these ethnic groups and when these effects first become apparent. The stage of life point is especially intriguing because another study has recently shown that when BAT function is assessed with thermal imaging, children (aged 6–11 years) who were non-Caucasian (but born in the UK) had more BAT than did white Caucasians.[8] Thus, whether changes in BAT growth and development through childhood and adolescence contribute to differences seen in young adulthood needs to be addressed. Such effects might not be confined to BAT because south Asians have a different overall growth trajectory, as indicated by adult bodyweight and height, which are both substantially lower than other populations (thus reflecting a different genotype as well as phenotype). Other factors that would be expected to affect BAT could include variations in the thermal environment and diet.[7] Molecular characteristics of BAT could offer further insights into the present controversy as to the different developmental origins of brown and white adipocytes and the relative contribution of beige adipose tissue to energy balance.[9] Finally, once BAT is lost (especially in early life) the question remains as to whether it can ever be reactivated or synthesised in sufficient amounts to affect whole-body energy balance.

As south Asians are much more susceptible to metabolic disturbances such as obesity and diabetes, it is important to establish whether these individuals are resistant to established stimulators of BAT thermogenesis such as chronic cold exposure or dietary stimulants like capsaicin.[10] This group is now the ideal target for new pharmacological interventions that might offer proof-of-principle that enhanced BAT volume or function can have long-term health benefits against metabolic disease.

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Stemming the tide of type 2 diabetes and its consequences in south Asian individuals

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Globally, individuals of south Asian descent have increased susceptibility to type 2 diabetes.[1] By age 80 years, 50% of south Asian migrants to the UK have diabetes,[2] with a younger age of onset and greater effect on cardiovascular outcomes than European comparators.[3]

What can be done to stem this tide? The Indian Diabetes Prevention Programme,[4] which studied more than 500 people with impaired glucose tolerance, showed a reduction of more than 25% in diabetes incidence over 2·5 years in those randomised to a lifestyle intervention or metformin, alone or in combination, compared with control. In the lifestyle intervention group, no weight loss was noted and increased physical activity seemed to account for the beneficial effects.[4]

In *The Lancet Diabetes & Endocrinology*, Raj Bhopal and colleagues[5] report outcomes of a family-based

intervention (PODOSA) in south Asian individuals with impaired glucose tolerance or impaired fasting glucose, living in the UK. This family-cluster randomised controlled trial was initially designed with incidence of diabetes at 3 years as its primary endpoint. Participants were randomised to an intensive lifestyle intervention (15 dietitian visits focussed on diet and physical activity) or control group (four dietitian visits with standardised advice on diet and physical activity). The intervention was culturally adapted and its acceptability to participants is borne out by impressive retention over 3 years. However, in view of unforeseen difficulties in recruitment of the planned 540 participants (because the frequency of impaired glucose tolerance and impaired fasting glucose was lower than expected), after 2 years of recruitment the primary endpoint was changed to weight loss, and only 171 participants were enrolled. At 3 years, there was a small reduction in weight in the intervention group compared with the control group (adjusted mean difference –1·64 kg [95% CI –2·83 to –0·44]). Although more participants in the intervention group lost weight, about 20% of participants in both groups gained more than 2·5 kg in weight. The number of participants achieving the recommended level of physical activity (≥30 min per day) did not differ significantly between groups (odds ratio [OR] 1·14 [95% CI 0·53–2·47]). While underpowered for this outcome, there was a suggestion of reduced incidence of diabetes in the intervention group compared with the control group (OR 0·68 [95% CI 0·27–1·67]).

Having engaged a south Asian population in PODOSA, it would have been informative to include an objective assessment of physical activity using monitors. Additionally, further useful information could have been gained with the inclusion of outcomes such as insulin concentration and bioimpedance measures of body fat and lean mass, which are simple and cost little to implement.

PODOSA showed that in a high-risk group of south Asian individuals, a lifestyle intervention resulted in weight loss. Could the modest weight loss achieved in PODOSA result in reduced progression to diabetes? Both the Finnish[6] and US[7] diabetes prevention trials (the former wholly, the latter largely consisting of participants of European origin), reported substantial reductions in progression to diabetes in response to lifestyle intervention. In both these trials, participants in the intervention groups achieved significant weight loss compared with those in the control groups (3·5 kg and 5·5 kg respectively), and major increases in physical activity. By contrast, in the Indian Diabetes Prevention Programme,[6] although participants in the lifestyle intervention group had substantially reduced progression to diabetes, they had no difference in weight change compared with participants in the control group. However, adherence to an exercise regimen requiring 30 min or more of daily brisk walking increased from 42% to 59%. It is surprising that PODOSA, with little change in physical activity, also hints at reduced progression to diabetes in response to lifestyle intervention (OR 0·68). But confidence limits around this estimate are wide (95% CI 0·27–1·67), and consistent with both a beneficial and harmful effect of the intervention, reflecting the too small sample size for this outcome, so that no definitive conclusions can be drawn. Alternatively, if the hint towards a reduction in diabetes is real, people from south Asia might be more responsive, in terms of diabetes progression, to weight loss than people of European origin. This intriguing hypothesis requires testing, and the planned longer term follow up of PODOSA could begin to address this question.


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What are the next steps for diabetes prevention research? In view of the fact that half of south Asian migrants will develop diabetes, many in early adulthood, an approach that targets high-risk individuals in late adulthood might be unrewarding. Additionally, there is evidence for transgenerational transmission of diabetes risk.[8] Future trials could adopt the family-based approach tested successfully in PODOSA, but recruit from the entire south Asian population and provide lifestyle advice to all, coupled with a more intense intervention, including medication, for those at highest risk (eg, overweight, family history).

Substantial lifestyle changes are difficult to maintain long term. Crucial periods of development have been identified that strongly contribute to adult disease, including pregnancy, infancy, and adolescence.[9] Animal and limited human data suggest that short-term interventions, including drugs, during these periods might greatly reduce or even eliminate the risk of disease.[10,11] Exploration of the effect of brief interventions during key periods of development offers a methodologically challenging, but potentially rewarding, alternative strategy to reduce the effect of diabetes in south Asian individuals.

Ultimately, the goal of any diabetes prevention strategy is to reduce the burden of complications and especially cardiovascular disease, which causes the most morbidity and mortality, and to which south Asian individuals are particularly susceptible. Endpoints should include cardiovascular risk factors and subclinical cardiovascular disease. Consideration of multiple risk factors should be as embedded in prevention trials as it now is in clinical practice.

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Cognitive decline in type 2 diabetes

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Evidence is accumulating that type 2 diabetes is associated with cognitive impairment and dementia. In individuals older than 60 years, 7–13% of dementia cases are estimated to be attributable to diabetes,[1] and the number of cases of diabetes-associated dementia is expected to increase because of the diabetes pandemic and ageing populations worldwide. Dementia is preceded by accelerated cognitive decline, and study of the risk factors for cognitive decline could therefore provide insights into the causes of dementia. However, the natural history of cognitive decline in type 2 diabetes is not well understood. Some researchers have suggested that clinically relevant cognitive decline related to type 2 diabetes does not develop until the neurodegenerative changes in the brain associated with ageing have started to occur (ie, after age 60 years).[1] Additionally, in some studies[2,3] the extent of cognitive decline in new-onset diabetes was not clearly different from that in individuals without diabetes, suggesting a threshold for diabetes duration in the association between cognitive decline and diabetes.

Against this background, Richard Tuligenga and colleagues' analysis[4] from the Whitehall II cohort study in *The Lancet Diabetes & Endocrinology* addresses the questions of whether type 2 diabetes is associated with cognitive decline before old age, and whether glycaemic control and disease duration are risk factors for faster cognitive decline. The investigators compared cognitive decline over 10 years between individuals with normoglycaemia, prediabetes, new-onset diabetes, and known diabetes; the known diabetes group had a mean age of 57·4 years—much younger than in previous studies (69–74 years).[2,5,6] They report that diabetes was associated with accelerated cognitive decline and that both disease duration and glycaemic control (assessed by HbA_{1c}) were important risk factors. A strength of the present study is that it explicitly compares the effect of diabetes with that of age. Cognitive decline in middle-aged individuals with diabetes was 1·24–1·45 times faster than that in normal ageing (ie, those with known diabetes had a 45% faster decline in memory [10 year difference in decline –0·13 SD, 95% CI –0·26 to –0·00; p=0·046] and a 24% faster decline in global cognitive score [–0·11 SD, –0·21 to –0·02; p=0·014]), which seems less than that in previous studies (1·5–2·0).[7] Because most previous studies were done in older individuals with diabetes, these findings suggest that the effect of diabetes on cognitive decline might accelerate with age. Thus, 10 years of diabetes could be calculated to correspond to 2·5–10 years of extra